REMARKS

The present Amendment and Response is being submitted together with a Request for Continued Examination (RCE). Applicants submit that their last Amendment and Response, filed on January 23, 2002, was examined and considered, as noted in the Advisory Action. Therefore, Applicants request that their last Amendment and Response and the subsequent Advisory Action be entered.

Applicants acknowledge the Examiner's determination in the Advisory Action that Applicants, with their last Amendment and Response, had overcome the new matter rejection and the indefiniteness rejection regarding the bonding in the P-X-R formula. Thus, the present Amendment and Response addresses only the rejections that were maintained and further explained in the Advisory Action.

Rejections under 35 U.S.C. § 112 for Indefiniteness of Addressability Practice

The rejection of Claims 1-19, 21-26, 28-39, and 67-89 under 35 U.S.C. § 112 was maintained based on the assertion that "the metes and bounds of addressability practice" are vague and indefinite. Specifically, it was asserted that U.S. Patent No. 5,632,957 columns 7-9, which the Applicants cited in support of the term "electronic addressability" in their last response, "failed to reveal a defining statement regarding addressability." In addition, it was noted that while the '967 patent describes "other addressable locations" at column 9, line 17, it does not state the basis for their addressability.

Applicants reiterate that U.S. Patent No. 5,632,957 was incorporated by reference into the present application. Moreover, Applicants again submit that the cited portions of the '967 patent provide a definition for the term "electronic addressability." The microlocations of the

microchip device of the present invention are defined in columns 7-9 of the '957 patent as particular locations on a microchip device that are associated with an electrode, a permeation layer, and attachment regions such that "when activated, a microlocation generates the free field electrophoretic transport of any charged functionalized specific binding entity towards the electrode." (See U.S.P. 5,632, 957, column 8, lines 1-28.) This description of the components of a microlocation and, in particular, the way in which the electrode associated with the microlocation causes the attachment of binding entities to the attachment region above the microlocation, defines the metes and bounds of the term "electronically addressable." Thus, the term "electronically addressable" is simply a succinct description of the addressing achieved by the use of electric fields that is described in detail in the '957 patent.

In addition, Applicants note that the "other addressable locations" referred to in column 9, line 17 refer to microlocations that store unreacted molecules or nonspecific analytes. As described in column 9, lines 10-18, these molecules and analytes are transported to particular microlocations using electric field transport. Specifically, when the desired reaction is completed, the electrode at the particular microlocation may have its potential reversed such that unreacted molecules are removed and, in some instances, stored at "other addressable microlocations." These "other" microlocations are described as addressable because their electrodes are biased opposite the previously referenced microlocations, and they are thus "addressed" with the unreacted molecules and non-specific analytes to store those entities at the other location. This is only logical as, when the previously referenced locations are biased, e.g., negatively, the repulsed charged biomolecules or unreacted molecules migrate towards the positively charged microlocation, where they are captured and stored.

Applicants also note that portions of the '957 patent in addition to those cited in their last response define the metes and bounds of the term "electronically addressable." For example, in column 4, lines 62-67, the electronic addressability of the microchip device and its microlocations, in particular, is described as follows:

> The basic device has a matrix of addressable microscopic locations on its surface; each individual micro-location is able to control electronically and direct the transport and attachment of specific binding entities (e.g., nucleic acids, enzymes, antibodies) to itself. All micro-locations can be addressed with their specific binding entities.

Similarly, electronic control of the attachment of specific binding entities to a particular microlocation is described in column 5, lines 65-67 and in column 6, lines 1-4:

> A controller for the device (or system) provides for individual control of various aspects of the device. When an APEX device or chip containing addressable microscopic locations is utilized, the controller permits individual microlocations to be controlled electronically so as to direct the transport and attachment of specific binding entities to that location.

These portions of the '957 patent define the electronic means by which binding entities are addressed to microlocations. Because addressability practice is defined in detail in the '957 patent, it is not vague or indefinite. Therefore, Applicants request that this rejection be reconsidered and withdrawn.

The rejection of Claims 1-19, 21-26, 28-39, and 67-89 under 35 U.S.C. § 112 was also maintained based on the assertion that the sections of the instant application that Applicants cited in their last response in support of the use of the term "electronic potential" in claim 6, 19, 26,

35, and 39 describe the control of pH and binding entity movement "without stating anywhere that this is addressability practice." It was also asserted that none of the claims include an addressability limitation regarding electrode potentials, but "leave it open for conjecture as to what is meant regarding addressability."

In response to these assertions, Applicants have amended claims 1, 14, 21, and 28 (the independent claims that correspond to dependent claims 6, 19, 26, 35, and 39), so that the independent claims expressly describe the relationship between "electronic addressability" and "electronic potential." Specifically, as amended, these claims expressly disclose that the addressing of biomolecules to specific microlocations results from a change in electronic potential. Applicants note that this amendment is fully supported by the specification. See, for example, column 6, lines 21-25 and column 9, lines 10-51 of U.S.P. 5,632,957, bearing in mind that the electrodes described in these specific parts are associated with a particular microlocation, as discussed in columns 7-9. Therefore, this amendment renders this rejection moot, and Applicants respectfully request that it be reconsidered and withdrawn.

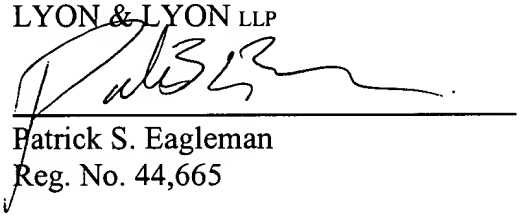
In addition, Applicants note that in claims 6, 19, 26, 35, and 39 the electronic potential produced at the electrode of a particular microlocation can be used for a purpose other than transporting or "addressing" a specific binding entity to the microlocation. Specifically, it can be used to form a localized concentration of acid or base at a particular electrode in order to activate reactive centers, thereby causing deposition chemistry to occur only at those specifically activated sites. See page 7, lines 19-31 and page 8, lines 1-5. Simply because a microlocation is electronically addressable does not mean that the electrode associated with it cannot be used for a purpose besides electronically induced transport of specific binding entities.

These remarks and amendments fully address and render moot the assertion that the addressability practice described in the claims at issue is indefinite and vague. Therefore, Applicants request that this rejection be reconsidered and withdrawn.

Based upon the foregoing amendments and remarks, Applicants respectfully submit that the application is now in condition for allowance. If the Examiner has any questions regarding this communication, or feels that an interview might facilitate prosecution of the application, he is invited to contact the undersigned at (949)567-2300.

Respectfully submitted,

LYON & LYON LLP

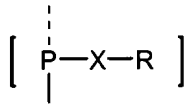
Dated: April 19, 2002 By: 

Patrick S. Eagleman
Reg. No. 44,665

633 West Fifth Street, Suite 4700
Los Angeles, California 90071-2066
(213) 489-1600 or (949) 567-2300

Version with Markings to Show Changes Made

1. (THRICE AMENDED) An electronically addressable microchip device comprising a plurality of electronically addressable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein biomolecules may be addressed to the microlocations by the application of an electronic potential to the microelectrode, and wherein at least some of the microelectrodes are covered by a permeation layer comprising at least a first chemical group for attaching to the microarray biomolecules, the first group having the formula:



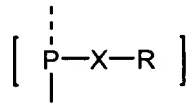
wherein,

P is a polymerizable moiety covalently attached to one or two moieties selected from the group consisting of: a monomeric unit of the permeation layer and another P-X-R group, as defined herein, wherein the other P-X-R group may be the same as or different from the first P-X-R group, further wherein the dashed line is a covalent bond to the second moiety if P is covalently attached to two moieties;

X is a covalent bond or a linking moiety; and

R is a functional moiety for attaching, either covalently or non-covalently, a derivatized biomolecule, or for attaching covalently another P-X-R group, as defined herein, wherein the other P-X-R group may be the same as or different from the first P-X-R group, and wherein R may, optionally, be attached to a biomolecule or another P-X-R group.

14. (THRICE AMENDED) An electronically addressable microchip device comprising a plurality of electronically addressable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein biomolecules may be addressed to the microlocations by the application of an electronic potential to the microelectrode, wherein at least some of the microelectrodes are covered by a permeation



layer comprising first and second chemical groups having the formula

wherein,

the dashed line is a covalent bond to a second moiety if P is covalently attached to two moieties

P is a polymerizable moiety,

X is a linking moiety selected from the group consisting of a covalent bond, an alkyl group of 1-10 carbon atoms, an alkenyl group of 2-10 carbon atoms, alkyl esters, ketones, ethers amides, thioesters, amido groups, and carbonyls, and any combinations thereof; and

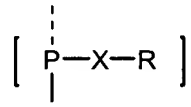
R is a functional moiety for attaching, either covalently or non-covalently, a derivatized biomolecule;

wherein the first and second P-X-R groups may be the same or different;

wherein the **P** moieties of the first P-X-R groups are covalently attached to the permeation layer matrix and to one **P** of the second P-X-R groups;

and wherein the **P** moieties of the second P-X-R groups are covalently attached to one or two other **P** moieties of other second P-X-R groups to form a polymer of the second P-X-R groups.

21. (THRICE AMENDED) An electronically addressable microchip device comprising a plurality of electronically addressable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein biomolecules may be addressed to the microlocations by the application of an electronic potential to the microelectrode, wherein at least some of the microelectrodes are covered by a permeation



layer comprising first P-X-R groups and second P-X-R groups having the formula:

wherein,

the dashed line is a covalent bond to a second moiety if P is covalently attached to two moieties;

P is a polymerizable moiety,

X is a linking moiety selected from the group consisting of a covalent bond, an alkyl group of 1-10 carbon atoms, an alkenyl group of 2-10 carbon atoms, alkyl esters, ketones, ethers amides, thioesters, amido groups, and carbonyls, and any combinations thereof; and

R is a functional moiety for attaching, either covalently or non-covalently, a derivatized biomolecule;

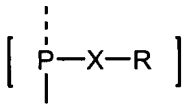
wherein the first and second P-X-R groups may be the same or different;

wherein the **P** moieties of the first P-X-R groups are covalently attached to the permeation layer matrix

wherein the **R** of the first P-X-R group is covalently attached to at least one **P** of the second P-X-R groups;

and wherein the **P** moieties of the second P-X-R groups are covalently attached to one or two other **P** moieties of other second P-X-R groups to form a polymer of the second P-X-R groups.

28. (THRICE AMENDED) An electronically addressable microchip device comprising a plurality of electronically addressable microlocations, wherein the microlocations each comprise an underlying working microelectrode on a substrate, wherein biomolecules may be addressed to the microlocations by the application of an electronic potential to the microelectrode, wherein at least some of the microelectrodes are covered by a permeation layer comprising first P-X-R groups attached to one or two moieties selected from the group consisting of biomolecules and polymerized monomer units comprising second P-X-R groups, wherein the polymerized second P-X-R groups are further attached to biomolecules, wherein the attachment of the biomolecules to the first P-X-R groups or to the polymerized second P-X-R groups requires activation of at least one of the first and/or the second P-X-R groups under acidic and/or basic pH conditions, wherein the first and second P-X-R groups have the formula



wherein,

the dashed line is a covalent bond to a second moiety if P is covalently attached to two moieties;

P is a polymerizable moiety, wherein;

X is a linking moiety selected from the group consisting of a covalent bond, an alkyl group of 1-10 carbon atoms, an alkenyl group of 2-10 carbon atoms, alkyl esters, ketones, ethers amides, thioesters, amido groups, and carbonyls, and any combinations thereof; and

R is a functional moiety for attaching, either covalently or non-covalently, a derivatized biomolecule or for attaching covalently an other P-X-R group;

wherein **P** comprises a chemical element requiring activation for attaching to the permeation layer and/or to a **P** of an other P-X-R group;

and wherein **R** comprises chemical elements requiring activation different from **P** of either the first or second P-X-R groups for attaching to biomolecules, or to **P** of another P-X-R groups.